Lipid But Not Glycaemic Parameters Predict Total Mortality from Type 2 Diabetes Mellitus in Canterbury, New Zealand

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A cohort of 447 subjects with Type 2 diabetes mellitus (208 male, 239 female; age range 30–82, median 62 years; and of predominantly European origin) was characterized in a clinic survey in 1989. Individual status (dead or alive) at 1 June 1995 was ascertained. Mortality rates were compared with the general New Zealand population by calculating standardized mortality ratios (SMR) and the hazard ratio (HR) of prognostic factors evaluated with Cox's proportional hazards model. At 6 years, 289 subjects were confirmed as alive and 133 as dead; only 25 were untraceable. Six-year survival for the cohort was 70 % (95 % CI 66–74). SMR was 2.53 (95 % CI 1.99–2.68) for the female cohort and 2.03 (95 % CI 1.60–2.59) for the male cohort. Factors assessed at baseline (1989) that were independently prognostic of total mortality included age, male sex, pre-existing coronary artery disease (CAD) (HR 2.2, 95 % CI 1.5–3.3) and plasma cholesterol (HR for 1.4 mmol l^{-1} change: 1.49, 95 % CI 1.2–1.9). HDL-cholesterol was protective in women (HR for 0.4 mmol l^{-1} change: 0.72, 95 % CI 0.51–1.00) but not men. Glycated haemoglobin was not a significant predictor of total mortality. Predictors of CAD mortality (in those subjects free of CAD in 1989) included plasma cholesterol (HR for 1.4 mmol l^{-1} change: 1.86 95 % CI 1.20–2.89), glycated haemoglobin (HR for 1.8 % change: 1.9 95 % CI 1.04–3.47), male sex, peripheral vascular disease, and smoking. There is therefore increased mortality in Type 2 diabetic subjects in Canterbury, New Zealand. HDL-cholesterol is protective against total mortality in females. © **1998 John Wiley & Sons, Ltd.**

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Introduction

Type 2 diabetes mellitus is associated with an increased mortality, predominantly from cardiovascular disease,[1–3] though with marked differences reported between countries and between underlying prognostic factors.[1–15] There are few data from New Zealand on mortality in Type 2 diabetes. Trends in mortality have been reported from 1966 to 1985 by Scragg,[16] but the data source was death certificate based and no distinction was made for the type of diabetes. Although mortality in the New Zealand general population from coronary heart disease has declined in the last 30 years,[17] the same trends need not necessarily have occurred in people with diabetes.

Improved glycaemic control has been shown to reduce incidence and prevent progression of microangiopathy in Type 1 diabetes,[18] and also to reduce cardiovascular events by 41%, although this was not statistically significant. Type 2 diabetes is characterized by a range of metabolic abnormalities that may be more important for atheromatous disease progression than hyperglycaemia *per se*,[19] and it remains to be established that tightened glycaemic control improves outcomes in Type 2 diabetes.[20] Whether glycaemic control has any relationship to mortality is open to debate with supporting evidence from some[13] but not other[14] studies. The role of glycaemic control in survival of adult-onset diabetes has not been fully substantiated, and it has been suggested that hyperinsulinaemia from insulin administration may promote atherogenesis.[21]

Other factors potentially influencing the prognosis of Type 2 diabetes subjects include attained age, diabetes duration, proteinuria, hypertension, dyslipidaemia, and smoking. Detailed study of such factors is essential if potential health returns form the many and expensive changes advocated for improved diabetes management[22]

Abbreviations: CAD coronary heart disease, HR hazard ratio, SMR standardized mortality ratio

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are to be accurately evaluated. We have studied the relationship between baseline clinical and demographic factors (recorded in 1989) and subsequent mortality in Type 2 diabetes in a New Zealand clinic population.

Patients and Methods

A clinic survey in 1989 identified a cohort of 447 subjects with Type 2 diabetes, defined as diabetes diagnosed after the age of 30 years and not requiring insulin within 1 year of diagnosis.

Factors detailed at baseline (defined as 1 June 1989) included age, sex, duration of diabetes, ethnicity, treatment modality for diabetes (diet, sulphonylurea, metformin, insulin or combination), body mass index (kg m^{-2}), smoking status, cholesterol (mmol l^{-1}), triglycerides (mmol l^{-1}), HDL-cholesterol (mmol l^{-1}), glucose (mmol l^{-1}), presence or absence of hypertension (defined as documented clinical diagnosis or on established anti-hypertensive medication), coronary artery disease (defined as any one of previous myocardial infarction, angina pectoris or coronary artery by-pass graft), retinopathy, neuropathy (absent ankle jerks or impaired sensation to the feet), peripheral vascular disease (absent foot pulses and/or symptomatic claudication), and albuminuria ($\geq$ 50 mg l^{-1}). Glycated haemoglobin was measured by an automated Furfural method,[37] and results divided by 10 to give a percentage equivalent to HbA_{1c} (non-diabetic range $<$ 5 %).

Survival status (dead or alive) at June 1 1995 was ascertained initially through clinic records at the Christchurch Hospital Diabetes Centre. Where subjects were found to be no longer under follow-up at the Diabetes Centre, contact was made with the general practitioner. Scrutiny of death notifications in local newspapers provided additional case identification and verification. Subjects untraced by the above methods (approximately 5 % of the study cohort) and those confirmed as deceased formed the basis of a secondary search process of the National Register of Deaths in New Zealand, in order to determine date, place, and cause of death. Death certificate records registered at local branches and at the National Office of the New Zealand Registrar of Births, Deaths and Marriages were reviewed.

Statistical Methods

Baseline variables (in 1989) were compared in those subjects confirmed as definitely alive on 1 June 1995 versus those identified as having died. Continuous variables were compared by 2-sample Student's *t*-test and after logarithmic transformation in those variables not normally distributed (triglycerides). Categorical variables were compared by chi-square testing.

Kaplan-Meier estimates of survival were computed (SAS Institute Inc., SAS/Stat software, Cary, North Carolina). In order to compare survival in the study cohort with that in the general population, single year of life probabilities were used from the New Zealand life tables 1990–92[23] to derive expected survival probabilities for a hypothetical cohort drawn from the general New Zealand population but matched to the study cohort for sex and age (single year of life).

Mortality was also compared with the general New Zealand population, by calculating standardized mortality ratios (SMR). The SMR compares the observed number of deaths in the diabetic population to that expected if the age-specific death rates of the general population applied to the number of person-years follow-up in each group in the study population. The age-sex specific mortality rates used in the calculations were single year of life mortality (or hazard) rates drawn from the 1990–92 New Zealand Life Tables.[23] For each individual in the study cohort, the appropriate age-sex specific mortality rates were obtained from the Life Tables for each year of follow-up contributed by that individual. Summing over individual years of follow-up gives the expected number of deaths for a hypothetical cohort drawn from the general population but matched to the study cohort for age and sex.

Cox's proportional hazards regression model was employed to evaluate the relative contributions of baseline variables to both total mortality and that attributable to coronary artery disease (SAS Institute Inc., SAS/Stat software). The hazard ratio (with 95 % confidence intervals) was determined for each variable included in the model, adjusted for the presence of all other variables, according to standard epidemiological practice.[24] In order to test proportional hazards assumptions the change in the model log-likelihoods (i.e. the improvement in fit) was examined when covariate by time interaction terms were included in the model.[25] This exercise was carried out for each covariate individually rather than jointly for all covariates in the full model, because of computative limitation. It was intended that time by covariate interaction terms would be included in the full model and the change in log-likelihood again assessed for any covariate for which there was evidence of non-proportionality in the single variable analyses. No evidence was found, however, of any non-proportionality in the single variate analyses. In order to check linearity assumptions for continuous covariates, log-likelihoods were compared between models with continuous variables represented as linear terms and those in which continuous covariates were represented as restricted cubic splines. For the all-cause mortality model, potential gender interactions were checked by first running separate analyses for males and females and then including in the final model gender by covariate interaction terms for those covariates which had significantly different effects in the two groups. Gender specific analyses were not undertaken for the CAD mortality models because these analyses were stratified by baseline CAD status and within each stratum there were too few deaths to explore interactions with gender.

Results

Of the 447 Type 2 diabetic subjects identified, 208 were male, 239 female, with age range 30–82, median 62 years. They were of predominantly European (95 %) origin. Clinical and demographic details are given in Table 1. Females had higher body mass index, total and HDL-cholesterol and glycated haemoglobin compared with male subjects at baseline in 1989. There were also significantly more hypertensive subjects in the female compared with the male group. At 6 years, 289 subjects were confirmed as alive and 133 as dead; 25 were untraceable. Cause of death was predominantly attributable to coronary artery disease (69 %), with remaining causes including malignancy (12 %), cerebrovascular disease (9 %), renal failure (2 %), and others including accidents, suicides and gastro-intestinal bleeding (10 %).

Baseline variables (in 1989) were compared in those subjects subsequently confirmed as definitely alive versus those subsequently identified as having died (Table 1). Those who subsequently died were older and had longer known duration of diabetes compared with those who survived. Those who subsequently died had lower baseline body mass index compared with survivors and higher total cholesterol, but were otherwise well-matched for metabolic variables. A significantly higher proportion of subjects had pre-existing cardiovascular and cerebrovascular disease compared with subsequent survivors and a higher proportion of albuminuria.

Kaplan-Meier curves are shown in Figure 1 for survival of the entire cohort (with 95 % confidence intervals) compared with the expected survival for a hypothetical age–sex matched sample from the general population. Five-year survival for the cohort was 74.0 % (95 % CI 70–78.0) and 6-year survival was 70 % (95 % CI 66–74).

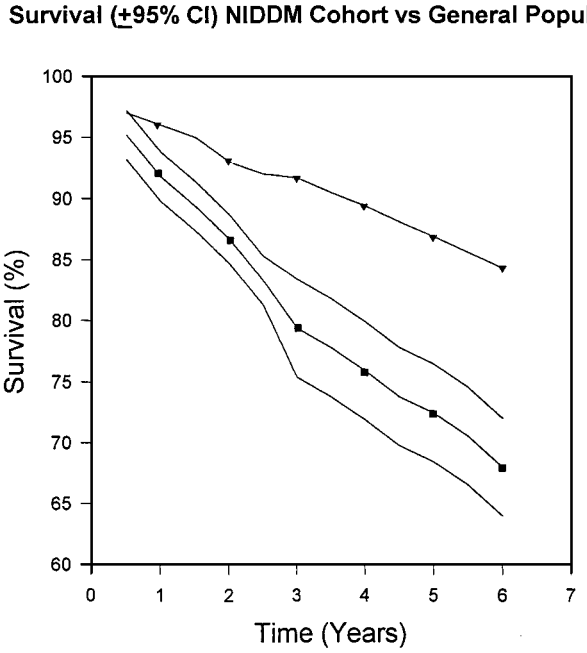

Figure 1. Kaplan–Meier curve for survival of the entire Type 2 diabetic cohort (with 95 % confidence intervals) compared with the expected survival for a hypothetical age-sex matched sample from the general population derived from Life Tables

Standardized Mortality Ratios (SMR with 95 % confidence intervals) are shown in Table 2 according to 10-year age bands and gender. SMR was 2.53 (95 % CI 1.99–2.68) for the female cohort overall and 2.03 (95 % CI 1.60–2.59) for the male cohort overall (Table 3). SMR tended to decline with advancing years in both sexes although it was still significant (greater than one) beyond the age of 70 years.

Factors at the baseline survey (in 1989) that were

Table 1. Clinical and demographic variables at baseline (1989) for male versus female subjects and for those identified as still alive in 1995 versus those having died

	Male ($n = 208$)	Female ($n = 239$)		Dead in 1995 ($n = 133$)	Alive in 1995 ($n = 289$)	
Age (yr)	61. ± 10.4	62.9 ± 10.2	NS	67.1 ± 8.1	60.3 ± 10.1	$p < 0.0001$
Duration (yr)	9.1 ± 7.6	10.0 ± 7.2	NS	11.9 ± 7.8	8.8 ± 7.0	$p < 0.0001$
BMI (kg m^{-2})	27.7 ± 4.1	29.0 ± 5.7	$p < 0.0001$	27.3 ± 4.5	28.9 ± 5.3	$p < 0.01$
Cholesterol (mmol l^{-1})	6.0 ± 1.3	6.5 ± 1.4	$p < 0.0001$	6.5 ± 1.6	6.2 ± 1.3	$p = 0.05$
Triglycerides (mmol l^{-1})	2.33 ±1.5	2.35 ± 1.5	NS	2.42 ± 1.45	2.30 ± 4.5	NS
HDL-Cholesterol mmol 1^{-1}	1.12 ± 0.4	1.28 ± 0.4	$p < 0.0001$	1.20 ± 0.43	1.21 ± 0.38	NS
Glycated haemoglobin (%)	6.1 ± 1.8	6.5 ± 1.9	$p < 0.01$	6.3 ± 1.8	6.3 ± 1.8	NS
Glucose (mmol l^{-1})	11.8 ± 4.8	12.6 ± 6.8	NS	13.2 ± 8.2	11.9 ± 4.73	$p = 0.1$
Albuminuria	23%	16%	$p = 0.09$	25%	17%	$p < 0.05$
Retinopathy	37%	45%	NS	46%	41%	NS
Coronary artery disease	27%	21%	NS	41%	16%	$p < 0.0001$
Hypertension	49%	62%	$p < 0.01$	59%	55%	NS
Smokers	16%	14%	NS	17%	14%	NS
Sex (male/female)				49%	45%	NS

Baseline clinical and demographic variables (in 1989) were compared in male versus female subjects for the entire Type 2 diabetic cohort and in those subjects subsequently confirmed as definitely alive versus those subsequently identified as having died. Baseline data from 25 subjects who were subsequently untraceable were excluded from the latter analysis. Continuous variables were compared by 2-sample Student's *t*-test and after logarithmic transformation in those variables not normally distributed (triglycerides). Categorical variables were compared by chi-square testing.

Table 2. Standardized mortality ratios for Type 2 diabetic subjects

Age	Observed deaths	Expected deaths	SMR	95 % CI (SMR)
Males				
< 50	3	0.73	4.11	1.32–12.7
50–59	9	3.58	2.52	1.31–4.84
60–69	30	12.23	2.45	1.72–3.51
≥ 70	24	15.93	1.51	1.01–2.25
Total	66	32.47	2.03	1.60–2.59
Females				
< 50	2	0.47	4.24	1.06–16.95
50–59	5	2.20	2.27	0.95–5.46
60–69	28	8.56	3.27	2.26–4.74
≥ 70	32	15.21	2.10	1.49–2.97
Total	67	26.44	2.53	1.99–3.21
Total (all)	133	58.91	2.26	1.90–2.68

The standardized mortality ratio (SMR) compares the observed number of deaths in the diabetic population to that expected if the age-specific death rates of the general population applied to the number of person-years follow-up in each group in the study population. The age-sex specific mortality rates used in the calculations were single year of life mortality (or hazard) rates drawn from the 1990–92 New Zealand Life Tables.

Table 3. Hazard ratios for total mortality

Variables (with changes used to determine hazards ratios)	Hazard ratio	95 % CI
Age (10 yr)	1.60	1.21–2.13
BMI (5 kg m^{-2})	0.90	0.69–1.18
Cholesterol (1.4 mmol l^{-1})	1.49	1.19–1.87
Glycated Hb (1.8 %)	0.95	0.73–1.25
Triglyceride (1.5 mmol l^{-1})	0.90	0.71–1.14
Glucose (6 mmol l^{-1})	0.96	0.70–1.32
Duration (7 yr)	1.2	0.98–1.47
Coronary artery disease	2.22	1.48–3.32
Cerebrovascular disease	1.88	1.00–3.52
Hypertension	1.33	0.88–2.02
Peripheral vascular disease	1.88	1.24–2.85
Metformin (cf. diet)	0.42	0.17–1.07
Sulphonylurea (cf. diet)	0.89	0.44–1.77
Combined oral (cf. diet)	1.35	0.69–2.66
Insulin (cf. diet)	1.01	0.55–1.85
Smoking	1.70	0.96–3.02
Peripheral neuropathy	1.17	0.76–1.81
Albuminuria	1.49	0.96–2.32
HDL-cholesterol (0.4 mmol l^{-1}) for males	1.09	0.87–1.38
HDL-cholesterol (0.4 mmol l^{-1}) for females	0.71	0.51–1.00

Cox's proportional hazards regression model was employed to evaluate the relative contributions of baseline variables (for changes indicated in parentheses) to total mortality. The risk ratio (with 95 % confidence intervals) was determined for each variable included in the model, adjusted for the presence of all other variables.

independently prognostic of total mortality are shown in Table 3. They include age, male sex, pre-existing cardiovascular disease (hazard ratio 2.2, 95 % CI 1.4–3.2) and plasma cholesterol level (hazard ratio 1.44, 95 % CI 1.2–1.8). A significant HDL by gender interaction was found ($X^2 = 4.70$, $1df$, $p = 0.03$) with the hazard ratio for total mortality (male compared with female) of 1.66 (95 % CI 1.08–2.56) at the median HDL level of 1.15 mmol l^{-1}, increasing to 2.90 (95 % CI 1.55–5.44) at the 90th centile for HDL of 1.67 mmol l^{-1}. Duration of known Type 2 diabetes, smoking, and presence of albuminuria were only weakly associated with outcome. Glycated haemoglobin and treatment modality were not significant predictors of total mortality.

For mortality attributable to coronary artery disease, there were differences in prognostic variables between those subjects free of CAD at baseline compared with those subjects with established CAD (Table 4). Where

CAD was already present in 1989, male sex and total cholesterol were significant predictors of mortality. BMI was also associated with outcome in this group ($X^2 = 14.07$, df2, $p < 0.001$), though the association was non-linear with increased relative risk at higher BMI levels (Table 4). In those subjects free of CAD at baseline, male sex and total cholesterol were also predictors of mortality, although BMI was not a significant predictor in this group. In addition, where CAD was not present at baseline, peripheral vascular disease, smoking and glycated haemoglobin also emerged as significant predictors of mortality.

Discussion

We have demonstrated increased total mortality in people with Type 2 diabetes mellitus in Canterbury, New Zealand, in both males and females, predominantly attributable to CAD. Higher standardized mortality ratios were found in the present study compared with many other studies as reviewed by Panzram,[9] and including those reported by Knuiman *et al*.[3] in a cohort of 906 rural, non-Aboriginal Australian subjects (1.83 for females, 1.43 for males). There is a marked variation, however, between centers for all-cause mortality in diabetes as reported in the WHO Multinational Study of Vascular Disease in Diabetics,[8] with a three-fold variation in mortality for men and four-fold for women. Caution needs to be exercised in comparing SMRs between populations as their primary function is to facilitate comparisons within populations.

The majority of studies find standardized mortality ratios to be higher for females than males,[3,7] as also observed in our study. Male sex was a significant predictor of total mortality in our cohort, even after correcting for the presence of other baseline variables. SMR also declines with age in our study, as reported in other studies,[3] although is still significant (greater than one) after the age of 70 in both males and females.

In our study, neither glycated haemoglobin nor random blood glucose at baseline were significant predictors of total mortality, although glycated haemoglobin was a predictor of CAD mortality in subjects free of CAD at baseline (Table 4). Our study group was clinic-based and likely to have better glycaemic control than that expected in the general population. Other study groups have however shown HbA_{1c} to be a predictor of CAD mortality.[3,4,12,13] Improved glycaemic conitrol has been shown to reduce incidence and prevent progression of microangiopathy in Type 1 DM[18] and to reduce cardiovascular events by 41 %, although this was not statistically significant. Type 2 diabetes is characterized by a range of metabolic abnormalities that may be more important for atheromatous disease progression than hyperglycaemia alone,[19] and it remains to be established that tightened glycaemic control improves outcomes in Type 2 diabetes.[20] Kuusisto *et al*.[12], in a 3.5-year follow-up study including 229 Type 2 diabetic subjects found that only HbA_{1c} at baseline and duration of diabetes predicted CHD death and all CHD events. In another prospective study from the same region of Eastern Finland, a 10-year follow-up of 133 newly diagnosed Type 2 diabetic subjects aged 65–74 years, both HbA_{1c} and fasting blood glucose were significant predictors of

Table 4. Hazard ratios[a] for CAD mortality by CAD status at baseline

	CAD FREE		CAD PRESENT	
	Hazard ratio	95 % CI	Hazard ratio	95 % CI
BMI (↑ 5 kg m^{-2})	1.05	0·65 to 1.71	1.45[b]	0·95 to 2.21
Cholesterol (↑ 1.4 mmol l^{-1})	1.86	1·20 to 2.89	1.87	1·04 to 3.35
HDL (↑ 0.4 mmol l^{-1})	1.13	0·85 to 1.52	0.61	0·31 to 1.13
Triglyceride (↑ 1.5 mmol l^{-1})	1.07	0·70 to 1.63	0.64	0·36 to 1.13
Ghb (↑ 1.8 %)	1.90	1·04 to 3.47	0.81	0·42 to 1.58
Glucose (↑ 6 mmol l^{-1})	0.48	0·23 to 1.01	0.84	0·46 to 1.53
Duration (↑ 7 yr)	1.36	0·92 to 2.01	1.28	0·82 to 2.01
Male sex	3.53	1·43 to 8.71	3.55	1·40 to 9.02
Cerebrovascular disease	0.81	0·14 to 4.77	2.38	0·69 to 8.20
Hypertension	1.69	0·75 to 3.82	1.80	0·72 to 4.50
PVD	4.37	1·88 to 10.15	2.23	0·92 to 5.36
Smoking	2.86	1·04 to 7.92	0.33	0·07 to 1.69
Peripheral neuropathy	0.68	0·26 to 1.75	1.67	0·69 to 4.03
Albuminuria (≥ 50 mg l^{-1})	1.86	0·80 to 4.33	1.00	0·36 to 2.75
Treat 1 (Met vs diet)	0.57	0·11 to 3.06	0.79	0·11 to 5.56
Treat 2 (Su vs diet)	0.90	0·26 to 3.12	1.26	0·26 to 6.154
Treat 3 (Su + Met vs diet)	1.02	0·29 to 3.64	4.25	0·85 to 21.31
Treat 4 (insulin vs diet)	0.84	0·27 to 2.67	1.97	0·43 to 9.00

[a]Adjusted for age and all other variables listed in the table.
[b]The BMI effect was non-linear so that the effect of an increment in BMI depends on BMI level. The hazard ratio reported in the table gives the effect of an increment of 5 kg m^{-2} for individuals with a BMI of 27, the median for individuals with pre-existing heart disease, i.e. the tabulated value gives the hazard ratio for comparing individuals with a BMI of 32 with individuals with a BMI of 27.

cardiovascular mortality in multiple regression analysis.[13] Sasaki,[4] in a systematic 20-year follow-up of 1221 Japanese diabetic patients found that early age of onset, retinopathy, albuminuria, and fasting blood glucose > 11.1 mmol l^{-1} predicted increased mortality. Such data might suggest that improved glycaemic control might have an influence on outcomes in Type 2 diabetes, although it could be contended that elevated blood glucose is a surrogate for other metabolic derangements in diabetes that are directly responsible for atherogenesis. The United Kingdom Prospective Study of Therapies of Maturity Onset Diabetes[20] is presently investigating the effect of improved glycaemic control on complications in Type 2 diabetes.

Our data provided no evidence that treatment with insulin was a significant predictor of mortality in the model employed. This is in contrast to other studies, such as that of Knuiman *et al*.[3] where subjects treated with insulin were found to have a worse prognosis, even after correcting for glucose and glycated haemoglobin, although the significance attributable to insulin treatment was lost when other factors were included in the regression model. Krolewski *et al*.,[26] in a retrospective analysis of 5210 diabetic patients found an increased mortality rate from coronary heart disease in men which was not related to mode of hypoglycaemic therapy, although in women the highest mortality was in the group treated with insulin. It is likely that there were many true Type 1 diabetic subjects in the cohort studied. It may be contended that those subjects on treatment with insulin are metabolically worse and unable to control their diabetes without insulin.

Several population-based prospective epidemiological studies, including the recently published Quebec Heart Study,[27] have reported an association between insulin and cardiovascular disease. It has also been postulated that insulin may have direct atherogenic effects on the arterial wall.[21] The question of whether endogenous insulin levels are a cardiovascular risk factor has major clinical implications for whether exogenous insulin might also increase cardiovascular risk. Preliminary data from the Veterans Affairs Cooperative Study suggested an increase in cardiovascular events in Type 2 diabetic subjects treated with intensive compared with standard regimes.[28] The issue of exogenous insulin therapy causing hyperinsulinaemia and its potential relationship with macrovascular disease[29] remains open to debate, although our data are reassuring in this respect. Similarly, sulphonylurea therapy was not found to be a predictor of mortality in our study. In the University Group Diabetes Program (UGDP), sulphonylurea therapy with tolbutamide was associated with increased cardiovascular mortality.[30] Although this study has been severely criticized on several grounds of design and conduct,[31] possible adverse outcomes with sulphonylurea therapy have never been completely disproved, although other studies from the United States[11] have found no difference in SMRs between cohorts of black diabetic patients treated with diet alone and another ethnically similar cohort, treated with either insulin and/or oral hypoglycaemic agents.

In one study from Eastern Finland,[14] HDL-cholesterol was the most powerful predictor of future CHD events in a 7-year follow-up study of 313 Type 2 diabetes subjects. The risk for CHD death was fourfold higher in Type 2 diabetes subjects with HDL-cholesterol < 0.9 mmol l.[14] Our data showed a protective effect of HDL-cholesterol in females but not males, and total cholesterol emerges as a potent predictor of total mortality in both sexes. In the present study, smoking, albuminuria (all grades), and known duration of Type 2 diabetes were weakly but not statistically significantly associated with total mortality in multivariate analysis and cannot be discounted as important factors in Type 2 diabetes survival. Studies from Denmark,[32] China,[33] and Britain[34] showed albuminuria to be a predictor of overall mortality, although in the WHO Multinational Study of Vascular Disease in Diabetes[35] significant excess mortality was demonstrated in patients without proteinuria.

We conclude that there is increased mortality in Type 2 diabetes in Canterbury, New Zealand. Despite changes in style and delivery of diabetes care introduced since the early 1980s,[36] there is an urgent need for better intervention strategies to lower these mortality rates.

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References

1. Stamler J, Vaccaro O, Neaton JD, Wentworth D for The Multiple Risk Factor Intervention Trial Research Group. Diabetes, other risk factors, and 12-year cardiovascular mortality for men screened in the multiple risk factor intervention trial. *Diabetes Care* 1993; **16**: 434–444.
2. Finch C, Zimmet P. Mortality from diabetes. In: Alberti KGMM, Krall LP, eds. *The Diabetes Annual/4*. Amsterdam: Elsevier 1988: 1–16.
3. Knuiman MW, Welborn TA, Whittall DE. An analysis of excess mortality rates for persons with non-insulin-dependent diabetes mellitus in Western Australia using the Cox proportional hazards regression model. *Am J Epidemiology* 1992; **135**: 638–646.
4. Sasaki A, Uehara M, Horiuchi N, Hasagawa K. A long-term follow-up study of Japanese diabetic patients: mortality and causes of death. *Diabetologia* 1983; **25**: 309–312.
5. Barrett-Connor E, Wingard DL. Sex differential in ischaemic heart disease mortality in diabetics: a prospective population-based study. *Am J Epidemiol* 1983; **118**: 489–496.
6. Zimmet PZ, Finch CF, Schooneveldt MG, King HO, Thoma K. Mortality from diabetes in Nauru: results of 4-yr follow-up. *Diabetes Care* 1988; **11**: 305–310.

7. Wong JSK, Pearson DWM, Murchison LE, Williams MJ, Narayan V. Mortality in diabetes mellitus: experience of a geographically defined population. *Diabetic Med* 1991; **8**: 135–139.
8. Head J, Fuller JH. International variations in mortality among diabetic patients: the WHO Multinational Study of Vascular Disease in Diabetes. *Diabetologia* 1990; **33**: 477–481.
9. Panzram G. Mortality and survival in type 2 (non-insulin dependent) diabetes mellitus. *Diabetologia* 1987; **80**: 123–131.
10. Kleinman JC, Donahue RP, Harris MI, Finucane FF, Madans JH, Brock DB. Mortality among diabetics in a national sample. *Am J Epidemiol* 1988; **128**: 389–401.
11. van der Zwaag R, Runyan JW, Davidson JK, Delcher HK, Mainzer I, Baggett HW. A cohort study of mortality in two clinic populations of patients with diabetes mellitus. *Diabetes Care* 1983; **6**: 341–346.
12. Kuusisto J, Mykkanen L, Pyorala K, Laakso M. Type 2 diabetes and its metabolic control predict coronary heart disease in elderly subjects. *Diabetes* 1994; **43**: 960–967.
13. Laakso M. Glycaemic control and the risk for coronary heart disease in patients with non-insulin-dependent diabetes mellitus: the Finnish Studies. *Ann Intern Med* 1996; **124**: 127–130.
14. Laakso M, Lehto S, Pentilla I, Pyorala K. Lipids and lipoproteins predicting coronary heart disease mortality and morbidity in patients with non-insulin-dependent diabetes. *Circulation* 1993; **88**: 1421–1430.
15. Welborn TA, Knuiman M, McCann V, Stanton K, Constable IJ. Clinical macrovascular disease in Caucasoid diabetic subjects: logistic regression analysis of risk variables. *Diabetologia* 1994; **27**: 568–573.
16. Scragg R. Secular trends in mortality from diabetes mellitus in New Zealand, 1966–1985. In: *Contemporary Health Issues*. Wellington: National Health Statistics Centre 1989: 23–27.
17. Hay DR. Recent statistical information on cardiovascular disease in New Zealand. In: *Heart Facts*. National Heart Foundation of New Zealand Technical Report Series 1996: 1–16.
18. The Diabetes Control and Complications Trial Research Group: The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 1993; **329**: 977–986.
19. Haffner SM, Stern M, Hazuda HP, Mitchell BD, Patterson JK. Cardiovascular risk factors in confirmed prediabetic individuals: does the click for coronary heart disease start ticking before the onset of clinical diabetes? *J Am Med Assoc* 1990; **263**: 2893–2898.
20. UK Prospective Diabetes Study. II: Reduction in HbA_{1c} with basal insulin supplement, sulfonylureas, or biguanide therapy in maturity-onset diabetes. *Diabetes* 1985; **34**: 793–798.
21. Stout RW. Insulin and atheroma: 20 year perspective. *Diabetes Care* 1990; **13**: 631–654.
22. New Zealand Society for the Study of Diabetes. Core components for a diabetes service. *NZ Med J* 1996; **108**: 434–435.
23. Statistics New Zealand. *New Zealand Life Tables 1990–1992*. Wellington: Statistics New Zealand, 1996.
24. Rothman K. *Modern Epidemiology*. Boston: Little Brown & Co., 1986.
25. Cox DR, Oakes D. *Analysis of Survival Data*. London: Chapman and Hall, 1984.
26. Krolewski AS, Czyzyk A, Janeczko D, Kopczynski J. Mortality from cardiovascular diseases among diabetics. *Diabetologia* 1997; **13**: 345–350.
27. Despres J-P, Lamarche B, Mauriege P, Cantin B, Dagenais GR, Moorjani S, Lupien P-J. Hyperinsulinaemia as an independent risk factor for ischaemic heart disease. *N Engl J Med* 1996; **334**: 952–957.
28. Abraira C, Johnson N, Colwell J, the VA CSDM Group. VA cooperative study on glycaemic control and complications in type II diabetes (VA CSDM): results of the completed feasibility trial (Abstract). *Diabetes* 1994; **43** (suppl): 59A.
29. Standl E, Janka HU. High serum insulin concentrations in relation to other cardiovascular risk factors in macrovascular disease of type 2 diabetes. *Horm Metab Res Suppl* 1985; **15**: 46–51.
30. University Group Diabetes Program. A study of the effects of hypoglycaemic agents on vascular complications in patients with adult onset diabetes. II Mortality Results. *Diabetes* 1970; **19** (suppl 2): 785–830.
31. Filo C, Miller JP, Williamson JR. The crux of the university's group diabetes programme. Spurious results and inappropriate data analysis. *Diabetologia* 1980; **18**: 179–185.
32. Gall MA, Borch-Johnsen K, Hougaard P, Nielsen FS, Parving HH. Albuminuria and poor glycaemic control predict mortality in Type 2 Diabetes. *Diabetes* 1995; **44**: 1303–1309.
33. Chan JC, Cheung CK, Cheung MY, Swaminathan R, Critchley JA, Cockram CS. Abnormal albuminuria as a predictor of mortality and renal impairment in Chinese patients with Type 2 Diabetes. *Diabetes Care* 1995; **18**: 1013–1016.
34. MacLeod JM, Lutale J, Marshall SM. Albumin excretion and vascular deaths in NIDDM. *Diabetologia* 1995; **38**: 610–616.
35. Wang SL, Head J, Stevens L, Fuller JH. Excess mortality and its relation to hypertension and proteinuria in diabetic patients. The World Health Organization Multinational Study of Vascular Disease in Diabetes. *Diabetes Care* 1996; **19**: 305–312.
36. Beaven DW, Scott RS. The organisation of diabetes care. In: *The Diabetes Annual/2*. Amsterdam: Elsevier 1986: 284–287.
37. Lever M, May PC, Andre C. Automated fluorimetric determination of furfurals. *Analytical Biochemistry* 1985; **144**: 6–14.

